

CLAIMS

What is claimed is:

1. A method of reducing the concentration of oxygen in an aqueous solution, comprising adding to the aqueous solution a reducing agent and a hemoprotein
5 having deoxygenase activity, and incubating the resulting solution under conditions suitable for deoxygenase activity.
2. A method of reducing the concentration of oxygen in an aqueous solution, comprising adding to the aqueous solution a reducing agent, a hemoprotein having deoxygenase activity and NO or a source of NO, and incubating the
10 resulting solution under conditions suitable for deoxygenase activity.
3. A method of consuming NO in an aqueous solution, comprising adding an NO-consuming hemoprotein to the aqueous solution in the presence of O₂ and a reducing agent, and incubating the resulting solution under conditions suitable for NO-consuming activity by the hemoprotein.
- 15 4. The method of Claim 3 wherein the NO-consuming hemoprotein is a flavohemoglobin.
5. A method of enzymatically reducing the concentration of oxygen in a mammal, comprising administering an effective amount of a hemoprotein having deoxygenase activity to said mammal.
- 20 6. The method of Claim 5 further comprising administering a reducing agent to said mammal.

7. The method of Claim 5 further comprising administering NO or a source of NO to said mammal.
8. The method of Claim 5 wherein said hemoprotein is a naturally occurring hemoprotein or an enzymatically active variant thereof.
- 5 9. The method of Claim 8 wherein said hemoprotein is selected from the group consisting of: *Ascaris* hemoglobin, myoglobin, a flavohemoglobin and an enzymatically active variant of any of the foregoing.
- 10 10. A method of enzymatically reducing the concentration of nitric oxide in a mammal, comprising administering an effective amount of an NO-consuming hemoprotein to said mammal.
11. The method of Claim 10 wherein said hemoprotein is selected from the group consisting of: *Ascaris* hemoglobin, myoglobin, a flavohemoglobin and an enzymatically active variant of any of the foregoing.
- 15 12. The method of Claim 10 wherein said hemoprotein is a bacterial flavohemoglobin.
13. A method of treating a mammal having a disorder characterized by pathologically proliferating cells, comprising administering a therapeutically effective amount of a hemoprotein having deoxygenase activity to said mammal.
14. The method of Claim 13 wherein the mammal has a tumor.
- 20 15. The method of Claim 13 wherein the mammal has prostatic hypertrophy or restenosis.

16. The method of Claim 13 further comprising administering a reducing agent to said mammal.
17. The method of Claim 16 wherein said reducing agent is selected from the group consisting of NADH, NADPH and a thiol.
- 5 18. A method of deoxygenating a tumor in a mammal, comprising administering a therapeutically effective amount of a hemoprotein having deoxygenase activity to said mammal.
- 10 19. The method of Claim 18 wherein said hemoprotein is selected from the group consisting of: *Ascaris* hemoglobin, myoglobin, a bacterial flavohemoglobin and an enzymatically active variant of any of the foregoing.
20. The method of Claim 18 further comprising administering a reducing agent to said mammal.
21. The method of Claim 20 wherein said reducing agent is selected from the group consisting of NADH, NADPH and a thiol.
- 15 22. A method of anti-tumor therapy, comprising administering a therapeutically effective amount of a hemoprotein having deoxygenase activity, and a therapeutically effective amount of one or more bioreductive cytotoxic agents to a mammal having a tumor.
- 20 23. The method of Claim 22 wherein said hemoprotein is selected from the group consisting of: *Ascaris* hemoglobin, myoglobin, a bacterial flavohemoglobin and an enzymatically active variant of any of the foregoing.

24. The method of Claim 22 further comprising administering a reducing agent to said mammal.
25. The method of Claim 24 wherein said reducing agent is selected from the group consisting of NADH, NADPH and a thiol.
- 5 26. The method of Claim 22 wherein said hemoprotein and said bioreductive cytotoxic agent are administered locally.
27. A method of potentiating the cytotoxic activity of a bioreductive cytotoxic agent, comprising administering a therapeutically effective amount of a hemoprotein having deoxygenase activity, or an enzymatically active fragment thereof, and a
10 therapeutically effective amount of said bioreductive cytotoxic agent to a mammal.
28. The method of Claim 27 wherein said hemoprotein is activated by NO.
29. The method of Claim 28 wherein said hemoprotein is selected from the group consisting of *Ascaris* hemoglobin, myoglobin, a flavohemoglobin and an
15 enzymatically active variant of any of the foregoing.
30. A method of enzymatically generating toxic reactive oxygen species in a mammal, comprising administering an effective amount of a hemoprotein to the mammal.
31. The method of Claim 30 wherein the hemoprotein is a flavohemoglobin.
- 20 32. The method of Claim 30 further comprising administering a reducing agent to said mammal.

33. The method of Claim 32 wherein said reducing agent is selected from the group consisting of NADH, NADPH and a thiol.
34. The method of Claim 30 wherein said reactive oxygen species is hydrogen peroxide or superoxide.
- 5 35. A composition comprising one or more hemoproteins having deoxygenase activity or NO-consuming activity, and a physiologically acceptable carrier.
36. The composition of Claim 35 further comprising one or more cytotoxic agents.
37. The composition of Claim 36 wherein at least one of said cytotoxic agents is a bioreductive toxic agent.
- 10 38. The composition of Claim 35 wherein at least one hemoprotein is a naturally occurring hemoprotein or an enzymatically active variant thereof.
39. The composition of Claim 35 wherein said hemoprotein is selected from the group consisting of *Ascaris* hemoglobin, a myoglobin, a flavohemoglobin and an enzymatically active variant of any of the foregoing.
- 15 40. The composition of Claim 35 wherein said composition further comprises a reducing agent.
41. The composition of Claim 40 wherein said reducing agent is NADH, NADPH or a thiol.

42. A method of treating a mammal infected with *Ascaris sp.*, comprising administering to said mammal a therapeutically effective amount of an inhibitor of NO synthase.
43. The method of Claim 42 wherein said inhibitor is selected from the group consisting of an L-arginine uptake inhibitor, arginase, NG-nitro-L-arginine, L-nitroarginine methyl ester, N-monomethyl-L-arginine, 2-ethyl-2-thiopseudourea, L-N6-(1-iminoethyl)lysine, aminoguanidine, and 7-nitroindazole.
44. A method of constricting blood vessels in a mammal, comprising administering to the mammal a hemoprotein.
45. A method of reducing blood flow in a tumor, comprising introducing into the tumor a hemoprotein.
46. A composition comprising a flavohemoglobin in a pharmaceutically acceptable vehicle.
47. The composition of Claim 46 wherein the flavohemoglobin is a bacterial flavohemoglobin.
48. The composition of Claim 46 wherein the flavohemoglobin is a yeast flavohemoglobin.
49. The composition of Claim 46 wherein the flavohemoglobin is *E. coli* flavohemoglobin.

50. A method for treating a disease or medical disorder in a mammal, comprising administering an effective amount of a flavohemoglobin to the mammal, wherein the disease or disorder is selected from the group consisting of inflammation, stroke, septic shock, arthritis, iritis, ulcerative colitis, acute
5 respiratory distress syndrome and heart failure.
51. The method of Claim 50 wherein the flavohemoglobin is administered by local injection.
52. The method of Claim 50 wherein the flavohemoglobin is administered intravenously.
- 10 53. The method of Claim 50 wherein the flavohemoglobin is from *Escherichia coli*.
54. The method of Claim 50 wherein the flavohemoglobin is from *Saccharomyces cerevisiae*.
55. A method for treating cancer in a mammal, comprising administering an effective amount of a flavohemoglobin to the mammal.
- 15 56. The method of Claim 55 wherein the flavohemoglobin is administered locally into a tumor.
57. A method for sensitizing a tumor of a mammal to radiation or chemotherapy, comprising administering an effective amount of a flavohemoglobin to the mammal.